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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,147	06/11/2001	Kenneth Kellar	NIDN-10	9771

22840 7590 03/14/2003

AMERSHAM BIOSCIENCES
PATENT DEPARTMENT
800 CENTENNIAL AVENUE
PISCATAWAY, NJ 08855

EXAMINER

HARTLEY, MICHAEL G

ART UNIT	PAPER NUMBER
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1616

DATE MAILED: 03/14/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/830,147

Applicant(s)

KELLAR, KENNETH

Examiner

Michael G. Hartley

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 February 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-14 and 23-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-14 and 23-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

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Response to Amendment

The amendment filed 2/03/2003 has been entered. Claims 1-4, 6 and 15-20 have been canceled. Claims 10-14 have been amended. New claims 23-32 have been added. Consequently, claims 10-14 and 23-32 are pending and have been examined herein.

Response to Arguments

Applicant's arguments with respect to claims 10-14 and 23-32 have been considered but are moot in view of the following new ground(s) of rejection. The amendments added that the Eu ion is specifically Eu(II), as well as, that the methods are specifically for imaging decreased vascular perfusion, thereby necessitating the following new grounds of rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-14 and 23-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Unger (US 5,368,840).

Unger discloses a method of imaging diseased vasculature (i.e., which would encompass regions of decreased vascular perfusion) comprising administering an MRI contrast agent comprising a physiologically tolerable Eu(II) compound, see column 9, lines 31-50 and column 6, lines 30-65. Unger discloses that the contrast agents include Eu(II) complexes with the same chelating agents as claimed, i.e., DOTA, EDTA, DO3A, kryptands, etc., see column 6, lines 36-56.. The Eu(II) may also be complexed to targeting moieties, such as polymers, antibodies, etc., as claimed, see column 6, lines 30-65. Given the limited number preferred metals listed, in which Eu(II) is specifically recited, as are the various chelates, as claimed, i.e., DOTA, DO3A, one reading the patent would at once envisage the use of Eu(II) chelates in the methods of MRI disclosed by Unger.

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Claims 10-12, 23-27, 29 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Lauffer (US 5,250,285).

Lauffer discloses a method of imaging diseased vasculature, including perfusion thereof, (i.e., which would encompass regions of decreased vascular perfusion) comprising administering an MRI contrast agent comprising a physiologically tolerable Eu(II) compound, see abstract, column 1, lines 50-64 and column 6, line 10+. Lauffer discloses that the contrast agents include Eu(II) complexes with the same chelating agents as claimed, i.e., DOTA, etc., see column 13, lines 50+ (which is a chelate having square planer symmetry as claimed). Given the limited number preferred metals listed, in which Eu(II) is specifically recited, as are the various chelates, as claimed, i.e., DOTA, DO3A, one reading the patent would at once envisage the use of Eu(II) chelates in the methods of MRI disclosed by Lauffer.

Note: The functional properties defined in claims 23 and 25-27 are inherent characteristics of the contrast agents. Since Unger and Lauffer disclose methods which are the same as that instantly claimed, e.g., methods of MRI using the same chelates as instantly claimed, e.g., DOTA Eu(II) complexes, such complexes would inherently be expected to have the same properties as claimed, e.g., relaxivities, changes in oxidative states and/or relaxivities by biological processes, etc.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 10-14 and 23-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over either one of Garrity (WO 95/07270, relying on US equivalent, 5,958,373) or Platzek (US 5,277,895) in view of either one of Unger (US 5,368,840) or Lauffer (US 5,250,285).

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Garrity discloses a method of generating a contrast enhanced image of a human or non-human animal subject comprising administering a MRI contrast agent thereto, see abstract and column 11, lines 23+, see abstract. The chelates contain europium, see column 11, lines 27-32 and claim 8. The chelates include various polychelates of DOTA, DO3A, etc., as claimed, see column 2+. The chelates are conjugated to a biological vector (e.g., an antibody, etc.) for *in vivo* targeting, see columns 9-10.

Platzek discloses a method of generating a contrast enhanced image of a human or non-human animal subject comprising administering a MRI contrast agent thereto, see abstract and column 11, lines 23+, see abstract and column 4, lines 33+. Platzek specifically discloses a europium chelate, see example 8, column 18. The chelates include DOTA compounds, etc., see column 3.

Garrity and Platzek teach the use of Eu complexes, but fail to specifically disclose that the Eu is EU(II). However, the use of Eu(II) as a paramagnetic metal in chelating agents for MRI contrast agents is well known in the art, and is also known as an equivalent to Eu(III) and other paramagnetic metals to provide an effective metal for MRI imaging as shown by Unger and Lauffer.

Unger and Lauffer teach that Eu(II) is a paramagnetic which is equivalent to other known paramagnetic metals and is a preferred metal for forming complexes with chelating agents to provide effective contrast agents for MRI, as shown above.

It would have been obvious to one of ordinary skill in the art to modify the methods disclosed by Garrity and Platzek to have used Eu(II) as the Eu metal ion because it is well known in the art that Eu(II) is a useful paramagnetic metal species which is equivalent to other paramagnetic metal species for use in MRI to provide effective contrast enhancement, as shown by Unger and Lauffer.

Claims 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable Unger (US 5,368,840) or Lauffer (US 5,250,285) in view of Rocklage (US 5,190,744).

While Unger and Lauffer teach that the MRI methods are useful for imaging various tissues, including tumors and/or the cardiovascular, they fail to specifically disclose that the methods are used for imaging the brain, such as, stroke, and the heart.

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Rocklage teaches that MRI is especially useful for imaging decreased blood perfusion, and can provide a quantitative and temporal determination of perfusion for imaging stroke (i.e., the brain), as well as, cardiovascular perfusion abnormalities, etc., see column 2.

It would have been obvious to one of ordinary skill in the art to employ the MRI methods disclosed by Unger or Laufer for imaging decreased perfusion in various tissue, including, the brain (i.e., stroke), cardiovascular system, etc., (as claimed) because it is well known in the art that MRI is especially useful for imaging such tissues because it provides a quantitative and temporal determination of perfusion for imaging stroke (i.e., the brain), as well as, cardiovascular perfusion abnormalities, etc., as shown by Rocklage.

Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael G. Hartley whose telephone number is (703) 308-4411. The examiner can normally be reached on M-F, 7:30-5, off alternative Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose G. Dees can be reached on (703) 308-4628. The fax phone numbers for the organization where this

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application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.


Michael G. Hartley
Primary Examiner
Art Unit 1616

MH
March 12, 2003